Background

- As almost 50% of people living with HIV are now >50 years old, long term survival is paramount.
- Osteoporosis is an increasing concern although not well-studied in this population.
- TAF is a tenofovir prodrug that maintains 90% lower tenofovir plasma levels than TDF resulting in less renal and bone toxicity.

Methods

Switch from TDF to E/C/F/TAF for Age ≥ 60

Multicenter, randomized, open-label, active control, 48-week study

- Eligibility criteria:
  - Age ≥ 60 years at baseline
  - HIV-1 RNA < 50 copies/mL at screening and for at least 6 months
  - No known resistance for TDF or 3TC/FTC
  - TDF user for ≥ 6 months on a TDF-containing 3 drug regimen
  - No history of osteoporosis
  - No known history of renal impairment

Disposition of Study Subjects: All Screened Subjects

Primary Endpoint: change in spine and hip BMD from baseline to Week 48

Key Exclusion Criteria

- Age < 60 years
- Currently receiving a TDF and FTC or FTC-containing (maximum 2 NRTIs) regimen
- History of treatment for ≥ 6 consecutive months prior to screening visit
- HIV-1 RNA > 50 copies/mL at screening and for at least 6 months
- One or more concomitant medications known to affect bone (e.g., bisphosphonates, aromatase, corticosteroids, griseofulvin, lenalidomide, and strontium ranelate)

Analysis

- Primary endpoint: percent change from Baseline to Week 48 in spine and hip BMD by DXA
- The percentage change from baseline in spine BMD at Week 48 was analyzed using an ANCOVA model, including treatment group and baseline spine BMD T-score (≤ 1.00 vs > 1.00) as a fixed effect in the model with baseline BMD and sex as covariates
- The spine and hip BMD were tested using the fallback procedure (to control for two primary endpoints) if spine BMD was statistically significant (α = 0.03), then the hip BMD was tested at 0.05 alpha level; if no statistically significant difference was found, then the hip BMD was tested at a 0.02 alpha level
- If no spine BMD value available, participant censored from primary analysis

Results

Change in Spine and Hip BMD Through Week 48

- No bone mineral density (BMD) gain with switching participants 60 years and older from a TDF- to a TAF-containing regimen.

Change in Diagnosis of Osteopenia or Osteoporosis Defined by T-Score

Baseline Characteristics

- No known resistance for TDF or 3TC/FTC
- TDF user for ≥ 6 months on a TDF-containing 3 drug regimen
- No history of osteoporosis
- No known history of renal impairment

Efficacy: change in BMD from baseline to Week 48

- Similar proportional of patients were on lipid-modifying medication
  - At baseline: E/C/F/TAF 37% (34%); TDF + (FTC or 3TC) + 3\% 18% (32%)
  - Initiated during study: E/C/F/TAF 3% (5%); TDF + (FTC or 3TC) + 2\% 1%

Adverse events and tolerability were also comparable

- AE leading to discontinuation were low in both arms

Conclusions

- Through W48, spine and hip BMD significantly increased in older participants who switched from TDF to TAF compared to those who continued a TDF-containing regimen.
- Slight 2.2% gain with TAF vs 0.1% loss with continued TDF (P < 0.001)
- Hip: 1.3% gain with TAF vs 0.7% loss with TDF (P < 0.001)
- No treatment-emergent fracture events reported

- Through W48, rates of virologic suppression were high in both groups
- Adis leading to discontinuation were low in both arms
- Adverse events and tolerability were also comparable between groups.
- Concentrations of renal biomarkers decreased more in those receiving a TAF-based regimen

The Week 48 BMD, efficacy and safety data support the switch from a TDF-containing regimen to E/C/F/TAF in suppressed HIV-infected participants aged > 60 years.